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FILING BY "EXPRESS MAIL" UNDER 37 CFR 1.10

EV 704617883 US Express Mail Label Number

A FIRST preliminary amendment.

15. A substitute specification.

14. An Application Data Sheet under 37 CFR 1.76.

16. A change of power of attorney and/or address letter.

A SECOND or SUBSEQUENT preliminary amendment.

18. A second copy of the published International Application under 35 U.S.C. 154(d)(4).

October 14, 2005

Date of Déposit

U. S. Department of Commerce Patent and Trademark Office Form PTO-1390-MOD (REV 10-96) ATTORNEY'S DOCKET NUMBER DC-4-33157A U.S. APPLICATION NO. (If known, see 37 CFR 1.5) TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) **CONCERNING A FILING UNDER 35 U.S.C. 371** INTERNATIONAL APPLICATION NO. INTERNATIONAL FILING DATE 16 APRIL 2004 18 APRIL 2003 PCT/EP04/004052 TITLE OF INVENTION METHODS FOR COMPOSITIONS TARGETING TYROSINE KINASES FOR THE DIAGNOSIS AND TREATMENT OF **OSTEOARTHRITIS** APPLICANT(S) FOR DO/EO/US DAOUTI, ET AL Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay 3. examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. A copy of the International Application as filed (35 U.S.C. 371(c)(2)) 5 \boxtimes is transmitted herewith (required only if not transmitted by the International Bureau). has been transmitted by the International Bureau. (See Form PCT/IB/308) c. is not required, as the application was filed in the United States Receiving Office (RO/US). A translation of the International Application into English (35 U.S.C. 371(c)(2)). Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C.371(c)(3)). are transmitted herewith (required only if not transmitted by the International Bureau). have been transmitted by the International Bureau. b. have not been made; however, the time limit for making such amendments has NOT expired. have not been made and will not be made. A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). An executed Declaration and Power of Attorney (original or copy) (35 U.S.C. 371(c)(4)). A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 10. 371(c)(5)). Items 11. to 16. below concern document(s) or information included. 11.
An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

17. A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825.

19. A second copy of the English language translation of the International application under 35 U.S.C. 154(d)(4).
 20. Other items or information: STATEMENT OF VERIFICATION RE: SUBMISSION OF SEQUENCE LISTING

INTERNATIONAL APPLICATIO PCT/EPO4/004052 DC-4-33157A CALCULATIONS PTO USE The following fees are submitted: \$300 21. Basic national fee..... **Examination Fee** 22. ☐ If International preliminary examination report was prepared by USPTO \$ \$200 23. Search fee If Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority. \$400 If International Search Report was prepared and provided to the Office. . . \$ All other situations..... 900 TOTAL OF 21, 22 AND 23 = Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$ for each additional 50 sheets of paper or fraction thereof. RATE Number of each additional 50 or fraction **Total Sheets** Extra sheets thereof (round up to a whole number) - 100 = /50 = \$ \$ for furnishing the oath of declaration later than Surcharge of \$ \$ months from the earliest claimed priority date (37 CFR 1.492(e)) NUMBER EXTRA RATE **CLAIMS** NUMBER FILED 900 18 50 \$ Total claims 38 - 20 = Х \$ 1,400 X 200 \$ 7 Independent claims 10 - 3 = S 360 MULTIPLE DEPENDENT CLAIM(S) (if applicable) 2,300 TOTAL OF ABOVE CALCULATIONS Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28). 2,300 SUBTOTAL = for furnishing the English translation later than 30 months from the Processing fee of \$ earliest claimed priority date (37 CFR 1.492(f)). 3,200 TOTAL NATIONAL FEE = Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$ per property 3,200 TOTAL FEES ENCLOSED = Amount to be: refunded charged to cover the above fees is enclosed. a. 🔲 A check in the amount of \$ Please charge Deposit Account No. 19-0134 in the name of Novartis in the amount of \$3,200 to cover the above fees. A b. 🛛 duplicate copy of this form is enclosed. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to с. 🛛 Deposit Account No. 19-0134 in the name of Novartis. NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status. Send all correspondence to the address associated with Customer No. 001095, which is currently: Thomas Digby Attorney for Applicants **Novartis** Corporate Intellectual Property Reg. No. L-0242 One Health Plaza, Building 104 (617) 871-3224 East Hanover, NJ 07936-1080 DATED: OCTOBER 14 , 2005